Remarks

The Office action mailed September 22, 2008, has been reviewed and carefully considered. Claims 26 and 29 have been amended. Support for these amendments can be found throughout the specification. No new matter has been added. Following entry of these amendments, claims 26-29, 36 and 41-59 are pending.

Sequence Listing

A replacement Sequence Listing that now includes a description of SEQ. ID. NO: 31 is submitted herewith.

35 U.S.C. §103 Rejections

Claims 26-29, 36, 41-46 and 55-59 have been rejected as allegedly obviousness over Simon *et al.* (*AIDS Res. And Hum. Retroviruses*, 17(10):937-952, 2001) combined with Tam (*PNAS*, 85(15): 5409-5413, 1988), Guertler *et al.* (U.S. Patent No. 6,566,513) and Kim *et al.* (*J. Immunol. Meth.* 257:51-54, 2001). Applicants respectfully traverse this rejection for at least the following reasons.

To establish a *prima facie* case of obviousness, the Office must establish that (1) there is some suggestion or motivation to combine the references, either in the references or in common general knowledge of one of skill in the art (MPEP § 2143.01); and (2) there is a reasonable expectation of success (MPEP § 2143.02). In addition, the Office must show that the references teach or suggest all claim limitations. "When determining whether a claim is obvious, an Examiner must make 'a searching comparison of the claimed invention – *including all its limitations* – with the teaching of the prior art.' Thus, 'obviousness requires a suggestion of all limitations in a claim.'" *Ex parte Mumper* BPAI, Appeal No. 2008-2332, June 27, 2008. The Office has failed to establish a *prima facie* case of obviousness for the presently pending claims, as described in detail below, at least because Simon *et al.* combined with the secondary references do not teach or suggest all claim limitations, there was no motivation to combine the references and combining the cited references do not result in the present invention as claimed.

Simon *et al.* describe the use of synthetic linear peptides directed at the gp41/36 and V3 regions of various lentivirus lineages in order to detect and differentiate the various lineages in human and non-human serum samples. The exemplified gp41/36 peptides disclosed in Simon *et al.* have 24 residues and the exemplified V3 residues have between 25-27 residues and are coated directly onto the walls of microtiter plates in the described immunoassays. As correctly noted in the September 22, 2008 Office action (page 6, item 13), Simon *et al.* do not teach multiple antigenic peptides (MAP) or peptide sequences of less than 16 amino acid residues. The importance of these two features is explained in the present specification at page 15, lines 6-17:

> "The specificity of peptides generally tends to increase as the length of the peptides decreases, but shorter peptides may also have reduced reactivity, which can reduce the sensitivity of the test. The MAP structure can compensate for this reduced sensitivity. In particular, the plurality of shorter linear peptides in the presently disclosed MAPs enables optimization for specificity and sensitivity. The specificity is enhanced by shorter linear peptide portions that are more antigenicity focused. The sensitivity is enhanced by the plurality of shorter linear peptides. For instance, the analytical discernability of the assay results is increased (*e.g.*, the optical density readout exhibits a more intense color). Although not bound by any theory, it is believed that since only a portion of the MAP molecule is in contact with the solid phase substrate, the other portions of the MAP molecule are free for antibody binding. In addition, MAPs provide increased antigen density, and thus an increased number of antibody binding sites per unit surface area."

Page 12, line 34 – page 13, line 1 of the specification also teaches that "[g]iven that longer peptides may give rise to non-specific reactivities outside or within primate lentiviruses, especially useful peptide sequences for MAP synthesis and assaying have less than about 16 amino acid residues per linear portion of each MAP."

Tam, Guertler *et al.* and Kim *et al.* (hereinafter referred collectively as secondary references) are relied upon by the examiner for teaching that it would have been obvious to

modify Simon *et al.* to include a MAP format and the disclosed antigenic sequences with less than 16 amino acid residues. However, for the reasons set out below, a person of ordinary skill in the art would not attempt to modify the teaching of Simon *et al.* as alleged by the examiner to arrive at the subject matter of the present claims and even if they did, such modification would not have yielded the present invention.

First, the assay described in Simon *et al.* is reported to be both highly specific and sensitive. Page 949, col. 1 states:

> The use of different gp41/36 peptides allowed us to identify all the positive samples in the reference human panel. None of the HIV-1/HIV-2-negative samples included in the reference panel reacted with any of the peptides included in our test. In the filed evaluation panels, the sensitivity of the gp41/36 peptide array, which was used as the detection component, was excellent: all the WB positive samples were detected by the gp41/36 component (100% sensitivity and 98% positive predictive value).

Therefore, the assays described in Simon *et al.* are sensitive enough to detect anti-lentivirus antibodies when they are present in both reference and filed samples and do not produce false negative results. It is abundantly clear that these assays do not suffer from the sensitivity problem which might be remedied by solutions proposed in Tam or Kim *et al.* As such, the skilled person would have no reason to modify the assay of Simon *et al.* as alleged by the examiner on page 7 of the instant office action.

Even if, for some reason the skilled person were to attempt to modify the assay of Simon *et al.* in light of the cited secondary references, the result would not be the subject-matter of the present claims. The skilled person would reformat the peptides of Simon *et al.* in a tandem repeat or multiple antigenic peptide format and the result would be tandem repeats or multiple antigenic peptides comprising gp41/36 peptides of 24 residues and V3 peptides of 25-27

residues. The skilled person would not employ antigenic sequences of less than 16 amino acid residues, as presently claimed.

The skilled person would not contemplate reducing the size of the peptides of Simon *et al.* because there is nothing in any of the cited references which might suggest that smaller peptides could effectively detect and differentiate isolates from different primate immunodeficiency virus (PIV) lineages. First, there is nothing in Simon *et al.* which might suggest to a skilled person the possibility that the gp41/35 and V3 peptides described might be reduced in length without compromising specificity or sensitivity. Second, there is nothing in any of the secondary references to cure this deficiency.

Guertler *et al.* relates to the immunodeficiency virus SIM27 of drill monkeys. Although, Guertler *et al.* disclose a 32-mer peptide SEQ ID NO: 31 derived from the cysteine loop region of gp41/gp36 of SIV-CPV that includes 11 amino acids of disclosed peptide SEQ ID NO: 1, nowhere do Guertler *et al.* suggest a MAP format or that antigenic sequences with less than 16 amino acid residues could be used to effectively detect and differentiate isolates from different PIV lineages.

Tam discloses several MAP constructs using various antigenic peptides (see Table I). However, none of the antigenic peptides are present in, derived from, or related to, a primate immunodeficiency virus. Moreover, Tam explored utilizing the MAP constructs for vaccines. There is no mention in Tam that MAP constructs could be utilized for diagnostic purposes, much less an enzyme immunoassay. Vaccines and immunoassays are quite different; one is therapeutic; the other is diagnostic. A person of ordinary skill in the art could not have reasonably predicted that an approach taken for a vaccine could be successfully applied in an immunoassay. The lack of connection to Simon *et al.* or the presently claimed immunoassay is especially apparent from the Tam's utter failure to even mention a PIV sequence or any applicability to PIV in general.

Although the sequences listed in Table 1 of Tam include less than 16 amino acid residues, there is nothing in Tam attributing any significance to the specific length of the

sequences. In other words, it is simply coincidence that the sequences of Tam are less than 16 amino acid residues long. Coincidence, of course, is an insufficient reason to find that it would have been obvious to combine references.

Kim *et al.* disclose the use of tandem repeats or multiple antigenic peptides as antigens to detect antibodies in immunoassays. Kim *et al.* employ a 13 residue HIV-1 peptide antigen in various formats to detect HIV-1 antibodies. However, there is no teaching about the binding of other lentiviruses, such as SIV or other PIVs to this antigen in any of these formats. In fact, Kim *et al.* is entirely silent with regard to detecting other lentiviruses or distinguishing between different lentivirus lineages. The skilled person would not reasonably expect on the basis of Kim *et al.* that peptide antigens of 13 residues would be useful in detecting and discriminating between divergent lentiviruses.

The present methods employ antigenic sequences of less than 16 residues. There is neither teaching nor suggestion in any of the cited references that antigenic sequences of this length could be used to both detect different PIV strains and discriminate between them, as described in the present application. One of ordinary skill in the art would not therefore attempt to modify the assays set out in Simon *et al.* in accordance with any of the cited secondary references. Even if the skilled person did attempt such modifications, the result would not fall within the present claims. As such, the Office has failed to established a *prima facie* case of obviousness and Applicants respectfully request the pending 35 U.S.C. §103(a) rejection be withdrawn.

Conclusion

It is respectfully submitted that the application is in condition for allowance. Should there be any questions regarding this application, examiner Snyder is invited to contact the undersigned attorney at the telephone number shown below.

Respectfully submitted,

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